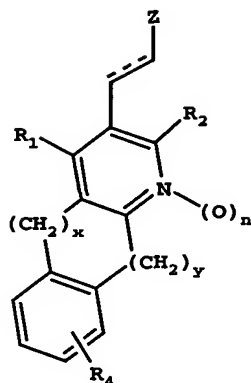
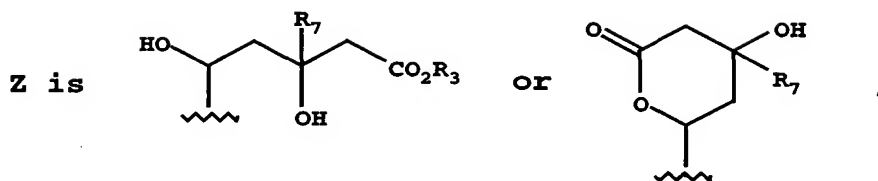


What is claimed is:

1. A compound having the structure



5 wherein



n is 0 or 1;

x is 0, 1, 2, 3 or 4;

10 y is 0, 1, 2, 3 or 4, provided that at least one of x and y is other than 0; and optionally one or more carbons of (CH₂)_x and/or one or more carbons of (CH₂)_y together with additional carbons form a 3 to 7 membered spirocyclic ring;

15 R₁ and R₂ are the same or different and are independently selected from alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl;

R₃ is H or lower alkyl;

20


R₄ is H, halogen, CF₃, hydroxy, alkyl, alkoxy, carboxyl, carboxyalkyl-, aminoalkyl, amino, alkanoylamino, aroylamino, cyano, alkoxyCON(R₁₀)-, R₁₁R₁₂NCO₂-, R₁₁R₁₂NCO-, R₁₃SO₂N(R₁₀)-, R₁₁R₁₂NSO₂N(R₁₀)-,
25 R₁₃OCO₂- or R₁₃OCO;

R₁₃ is alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroaryl;

R₁₁ and R₁₂, and R₁₀ are the same or different and are independently selected from H, alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl;


5 or R₁₁ and R₁₂ may be taken together with the nitrogen to which they are attached to form a stable 3 to 8 membered ring, which, where applicable, includes 1 to 3 heteroatoms in the ring.

R₇ is H or lower alkyl;

10 and  represents a single bond or a double bond (which may be cis or trans);

and pharmaceutically acceptable salts thereof (when R₃ is H), esters thereof, prodrug esters thereof, and all stereoisomers thereof.

15

2. The compound as defined in Claim 1 wherein  is a double bond which is trans.

20 3. The compound as defined in Claim 1 wherein Z is in the form of a pharmaceutically acceptable basic salt.

4. The compound as defined in Claim 1 in the form of a pharmaceutically acceptable acid addition salt.

25 5. The compound as defined in Claim 1 wherein R₁ and R₂ are independently selected from alkyl, cycloalkyl and aryl;

R₄ is H or halogen;

n is 0;

30 x is 2 or 3;

and y is 0.

6. The compound as defined in Claim 1 wherein R₁ is aryl,


35 R₂ is alkyl or cycloalkyl;

R₄ is H;

n is 0;

x is 3;


y is 0; and

5  is a trans double bond, in the form of a free acid, an alkali metal salt, or an alkaline earth metal salt, or an amino acid salt.

7. The compound as defined in Claim 6 wherein R₁ is phenyl which contains 1 or 2 substituents,

R₂ is alkyl or cycloalkyl;

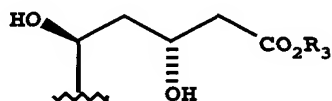
10 R₄ is H; and

 is a trans double bond, in the form of a free acid, an alkali metal salt, or an alkaline earth metal salt or an amino acid salt.

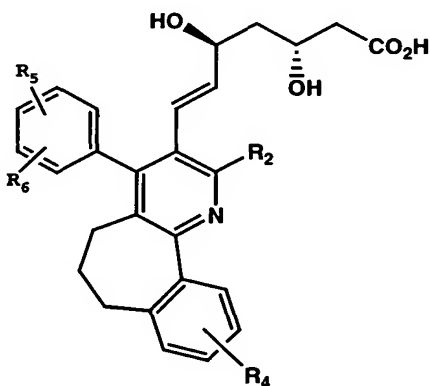
15 8. The compound as defined in Claim 7 wherein R₁ is 4-fluorophenyl, 4-fluoro-3-methylphenyl, or 3,5-dimethylphenyl; and

R₂ is isopropyl, t-butyl or cyclopropyl.

20 9. The compound as defined in Claim 1 wherein Z has the structure



25 10. The compound as defined in Claim 1 having the structure

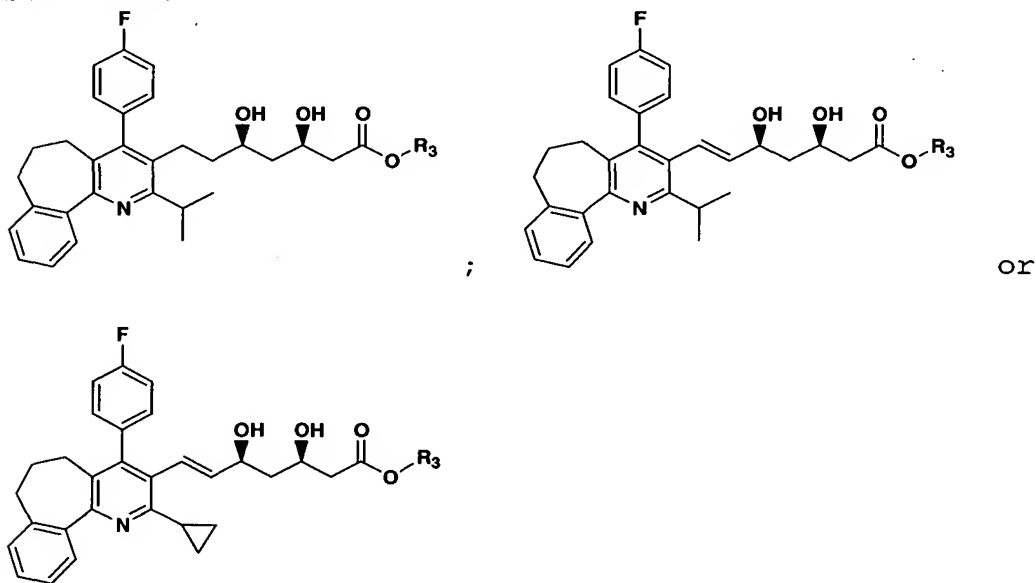


or an alkali metal salt, or an alkaline earth metal salt,
or an amino acid salt, or an acid addition salt via the
pyridine of the corresponding δ lactone,

wherein R_5 and R_6 are the same or different and are
5 independently selected from H, halogen or alkyl and
 R_2 is alkyl or cycloalkyl.

11. The compound as defined in Claim 10 wherein R_5
and R_6 are H and 4-fluoro;
10 H and 4-fluoro-3-methyl or
3,5-dimethyl; and
 R_2 is isopropyl, t-butyl or cyclopropyl.

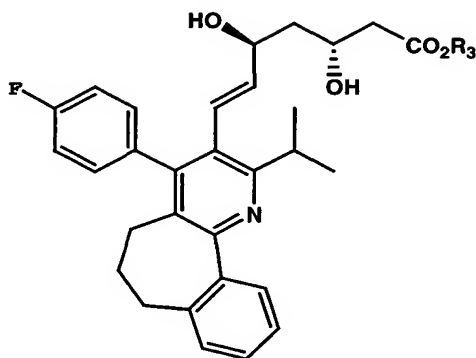
12. The compound as defined in Claim 1 having the
15 structure



wherein R_3 is H or an alkali metal, alkaline earth metal,
20 amino acid salt, or other pharmaceutically acceptable
salt, or the internal lactone thereof.

13. The compound as defined in Claim 1 in the form
of its calcium salt, sodium salt or arginine salt.
25

14. A compound of the structure



wherein R_3 is H or an alkali or alkaline earth metal ion
5 or an amino acid, or the internal lactone thereof.

15. The compound as defined in Claim 14 in the
form of its sodium salt, calcium salt or arginine salt.

10 16. A pharmaceutical composition comprising a
compound as defined in Claim 1 and a pharmaceutically
acceptable carrier therefor.

15 17. A pharmaceutical combination comprising the
HMG CoA reductase inhibitor compound as defined in Claim
1 and one or more hypolipidemic agents or lipid-lowering
agents, or lipid agents, or lipid modulating agents,
and/or one or more other types of therapeutic agents
including antidiabetic agents, anti-obesity agents,
20 antihypertensive agents, platelet aggregation inhibitors,
anti-dementia agents, anti-Alzheimer's agents, anti-
osteoporosis agents, and/or hormone replacement
therapeutic agents, and/or other cardiovascular agents
(including anti-anginal agents, anti-arrhythmic agents,
25 anti-atherosclerosis agents, anti-inflammatory agents,
anti-arthritis agents, anti-platelet agents, anti-heart
failure agents), anti-cancer agents, anti-infective
agents, hormone replacement agents, growth hormone
secretagogues, selective androgen receptor modulators,
30 and/or immunomodulatory agents.

18. The combination as defined in Claim 17 wherein the hypolipidemic agent or lipid-lowering agent or other lipid agent or lipid modulating agent or anti-
5 atherosclerotic agent, which is employed comprises 1,2,3 or more MTP inhibitors, HMG CoA reductase inhibitors, squalene synthetase inhibitors, fibric acid derivatives, PPAR α agonists, PPAR dual α/γ agonists, PPAR δ agonists, ACAT inhibitors, lipoxygenase inhibitors, cholesterol
10 absorption inhibitors, ileal Na⁺/bile acid cotransporter inhibitors, upregulators of LDL receptor activity, cholesteryl ester transfer protein inhibitors, bile acid sequestrants, or nicotinic acid and derivatives thereof, ATP citrate lyase inhibitors, phytoestrogen compounds, an
15 HDL upregulators, LDL catabolism promoters, antioxidants, PLA-2 inhibitors, antihomocysteine agents, HMG-CoA synthase inhibitors, lanosterol demethylase inhibitors, or sterol regulating element binding protein-I agents.

20 19. The pharmaceutical combination as defined in Claim 17 comprising said HMG CoA reductase inhibiting compound and an antidiabetic agent.

20. The combination as defined in Claim 19 wherein
25 the antidiabetic agent which may be optionally employed is 1,2,3 or more antidiabetic agents or antihyperglycemic agents including insulin secretagogues or insulin sensitizers, which may include biguanides, sulfonyl
ureas, PTP-1B inhibitors, aldose reductase inhibitors,
30 glucosidase inhibitors, PPAR γ agonists, PPAR α agonists, PPAR δ antagonists or agonists, aP2 inhibitors, PPAR α/γ dual agonists, dipeptidyl peptidase IV (DP4) inhibitors, SGLT2 inhibitors, glycogen phosphorylase inhibitors, and/or meglitinides, insulin, and/or glucagon-like
35 peptide-1 (GLP-1) or a mimetics thereof.

21. The combination as defined in Claim 20 wherein the antidiabetic agent is 1, 2, 3 or more of metformin, glyburide, glimepiride, glipyrider, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, pioglitazone, troglitazone, rosiglitazone, insulin, G1-262570, isaglitazone, JTT-501, NN-2344, L895645, YM-440, R-119702, AJ9677, repaglinide, nateglinide, KAD1129, AR-HO39242, GW-409544, KRP297, AC2993, LY315902, P32/98 and/or NVP-DPP-728A.

10

22. The combination as defined in Claim 17 wherein the HMG CoA reductase inhibiting compound is present in a weight ratio to the lipid-lowering agent or antidiabetic agent within the range from about 0.001:1 to about 100:1.

15

23. The combination as defined in Claim 17 wherein the other type of therapeutic agent which may be optionally employed is 1, 2, 3 or more of an anti-obesity agent which is a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin (and dopamine) reuptake inhibitor, an aP2 inhibitor, a thyroid receptor beta drug, an anorectic agent, a PTP-1B inhibitor, a CCKA agonist, a neuropeptide Y antagonist, a melanocortin-4-receptor agonist, a PPAR modulator which is a PPAR γ antagonist, PPAR α agonist, and/or PPAR δ antagonist, a leptin inhibitor such as a leptin receptor activator, a fatty acid oxidation upregulator or inducer.

20

25

24. The combination as defined in Claim 23 wherein the anti-obesity agent is orlistat, ATL-962, AJ9677, L750355, CP331648, sibutramine, topiramate, axokine, dexamphetamine, phentermine, phenylpropanolamine, and/or mazindol, P57 or CP-644673 (Pfizer).

30

25. The combination as defined in Claim 17 wherein the lipid modulating agent is an MTP inhibitor, an HMG

35

CoA reductase inhibitor, a squalene synthetase inhibitor, a fibric acid derivative, an upregulator of LDL receptor activity, a lipoxxygenase inhibitor, or an ACAT inhibitor and the other lipid agent is a cholesteryl ester transfer
5 protein inhibitor.

26. The combination as defined in Claim 25 wherein the lipid modulating agent is pravastatin, lovastatin, simvastatin, atorvastatin, cerivastatin, fluvastatin,
10 pitavastatin, rosuvastatin, fenofibrate, gemfibrozil, clofibrate, avasimibe, TS-962, MD-700, cholestagel, niacin, and/or LY295427.

27. The combination as defined in Claim 17 wherein
15 the antihypertensive agent employed is an ACE inhibitor, angiotensin II receptor antagonist, NEP inhibitor, a NEP/ACE inhibitor, a calcium channel blocker, a T-channel calcium antagonist, a β -adrenergic blocker, a diuretic, a α -adrenergic blocker, a dual action receptor antagonist
20 (DARA), or a heart failure drug.

28. The combination as defined in Claim 27 wherein the antihypertensive agent is an ACE inhibitor which is captopril, fosinopril, enalapril, lisinopril, quinapril,
25 benazepril, fentiapril, ramipril or moexipril;

an NEP/ACE inhibitor which is omapatrilat, gemopatrilat, or CGS 30440;

an angiotensin II receptor antagonist which is irbesartan, losartan or valsartan;

30 amlodipine besylate, prazosin HCl, verapamil, nifedipine, nadolol, propranolol, or clonidine HCl, carvediol, atenolol, hydrochlorothiazide, torasemide, furosemide, spironolactone or indapamide.

35 29. The combination as defined in Claim 17 wherein the HMG CoA reductase inhibitor is in combination with an ACE inhibitor or a NEP/ACE inhibitor.

30. The combination as defined in Claim 17 wherein the HMG CoA reductase inhibitor is in combination with an ACE inhibitor which is ramipril.

5

31. The combination as defined in Claim 17 wherein the HMG CoA reductase inhibitor is in combination with a NEP/ACE inhibitor which is omapatrilat or gemopatrilat.

10

32. The combination as defined in Claim 17 wherein the HMG CoA reductase inhibitor is in combination with a platelet aggregation inhibitor.

15

33. The combination as defined in Claim 32 wherein the platelet inhibitor is clopidogrel.

20

34. The combination as defined in Claim 32 wherein the platelet inhibitor is clopidogrel, aspirin or a combination of clopidogrel and aspirin.

25

35. The combination as defined in Claim 17 wherein the platelet aggregation inhibitor is aspirin, clopidogrel, ticlopidine, dipyridamole, ifetroban, abciximab, tirofiban, eptifibatide, or anagrelide.

30

36. The combination as defined in Claim 17 wherein the other therapeutic agent is an anti-Alzheimer's agent or anti-dementia agent, which is tacrine HCl (Cognex®), donepezil (Aricept®), a γ -secretase inhibitor, a β -secretase inhibitor and/or antihypertensive agent;

an antiosteoporosis agent, which is parathyroid hormone, a bisphosphonate, alendronate, a Ca receptor agonist or a progestin receptor agonist;

35

a hormone replacement therapeutic agent, which is a selective estrogen receptor modulator (SERM);

a tyrosine kinase inhibitor;

a selective androgen receptor modulator;

an antiarrhythmic agent, which is a β -blocker, or a calcium channel blocker, or an α -adrenergic blocker;

coenzyme Q sub. 10;

an agent that upregulates type III endothelial cell
5 nitric acid syntase;

a chondroprotective compound which is polysulfated glycosaminoglycan (PSGAG), glucosamine, chondroitin sulfate (CS), hyaluronic acid (HA), pentosan polysulfate (PPS), doxycycline or minocycline;

10 a cyclooxygenase (COX)-2 inhibitor, which is Celebrex® (Searle) or Vioxx® (Merck) or a glycoprotein IIa/IIIb receptor antagonist;

a 5-HT reuptake inhibitor;

a growth hormone secretagogue;

15 an anti-atherosclerosis agent;

an anti-infective agent, or an immunosuppressant for use in transplantation, or an antineoplastic agent.

37. A method for treating hypercholesterolemia,
20 dyslipidemia, hyperlipidemia, hyperlipoproteinemia, LDL Pattern B, LDL Pattern A, hypertriglyceridemia or atherosclerosis, or Alzheimer's disease or osteoporosis, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a
25 compound as defined in Claim 1.

38. A method of inhibiting cholesterol biosynthesis or lowering blood serum cholesterol levels and/or modulating blood serum cholesterol levels, lowering LDL
30 cholesterol and/or increasing HDL cholesterol, or treating dyslipidemia, mixed dyslipidemia, LDL Pattern B, LDL Pattern A, hyperlipidemia, hypercholesterolemia, hypo α -lipoproteinemia, hyperlipoproteinemia or hypertriglyceridemia, and other aberrations of
35 apolipoprotein B metabolism, or reducing levels of Lp(a), or treating or preventing other cholesterol-related diseases, or treating or preventing or reversing

progression of atherosclerosis, or preventing or treating Alzheimer's disease, or preventing or treating osteoporosis and/or osteopenia, or reducing inflammatory markers, reducing C-reactive protein, or preventing or
 5 treating low grade vascular inflammation, or preventing or treating stroke, or preventing or treating dementia, or preventing and treating coronary heart disease, and primary and secondary prevention of myocardial infarction, or preventing or treating stable and unstable
 10 angina, or primary prevention of coronary events, or secondary prevention of cardiovascular events, or preventing or treating peripheral vascular disease, preventing or treating peripheral arterial disease, or preventing or treating acute vascular syndromes, or
 15 preventing or reducing the risk of undergoing myocardial revascularization procedures, or preventing or treating microvascular diseases such as nephropathy, neuropathy, retinopathy and nephrotic syndrome, or preventing or treating hypertension, which comprises administering to a
 20 mammalian species in need of treatment a therapeutically effective amount of a compound in accordance with Claim 16.

39. A method for preventing or treating diabetes,
 25 especially Type 2 diabetes, and related diseases, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, obesity, LDL Pattern B, LDL Pattern A, Syndrome X, diabetic complications, dysmetabolic syndrome, and related
 30 diseases, and sexual dysfunction, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

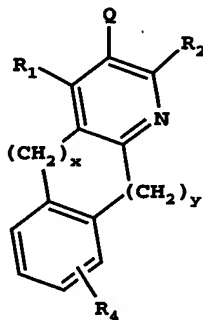
35 40. A method for preventing and treating malignant lesions, premalignant lesions, gastrointestinal malignancies, liposarcomas and epithelial tumors, cancer-

induced asthenia (fatigue), irritable bowel syndrome, Crohn's disease, gastric ulceritis, and gallstones, and HIV infection, drug-induced lipodystrophy, and proliferative diseases, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

41. A method for improving coagulation homeostasis, reducing PAI-1 activity, reducing fibrinogen, and/or reducing platelet aggregation, and/or improving endothelial function, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

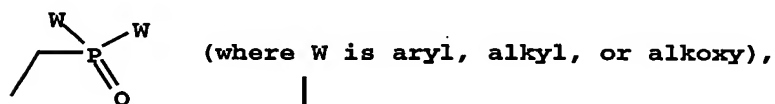
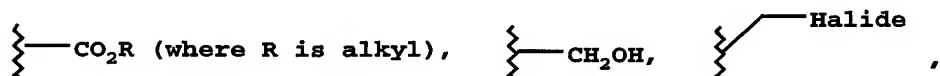
42. A method for treating cholesterol related diseases, diabetes and related diseases, cardiovascular diseases, cerebrovascular diseases, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of a combination of a compound as defined in Claim 1 and a hypolipidemic agent, and/or lipid modulating agent and/or antidiabetic agent and/or cardiovascular agent, cerebrovascular agent, and/or other type of therapeutic agent, which comprises administering to a mammalian species in need of treatment a therapeutically effective amount of such combinations.

43. A compound having the structure

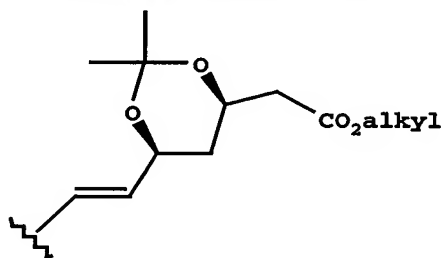


wherein R_1 and R_2 are the same or different and are independently selected from alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl or cycloheteroalkyl; Q is

5

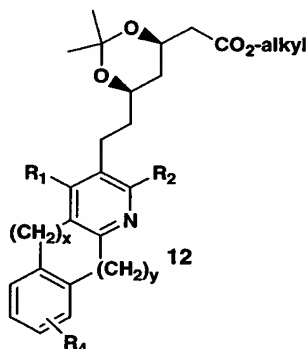
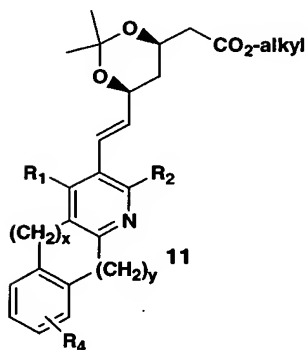
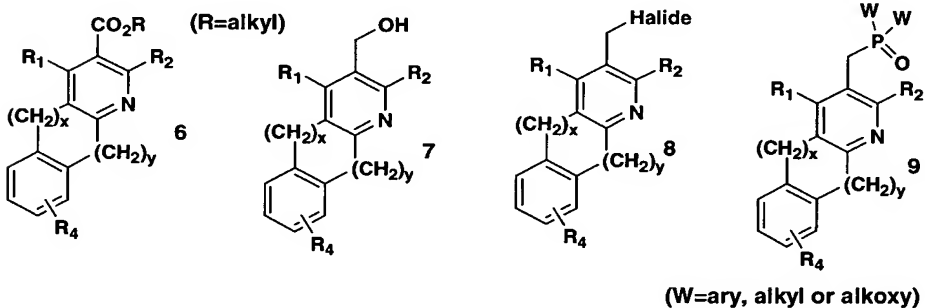


or

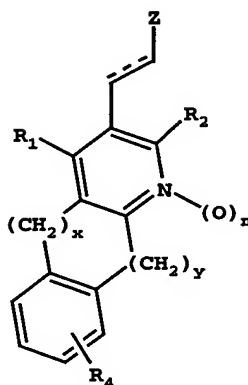


44. The compound as defined in Claim 43 having the following structures:

10

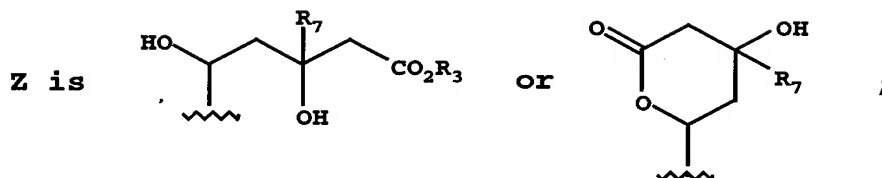


45. A compound having the structure



wherein

5



n is 0 or 1;

x is 0, 1, 2, 3 or 4;

y is 0, 1, 2, 3 or 4, provided that at least one of
 10 x and y is other than 0; and optionally one or more
 carbons of (CH₂)_x and/or one or more carbons of (CH₂)_y
 together with additional carbons form a 3 to 7 membered
 spirocyclic ring;

R₁ and R₂ are the same or different and are
 15 independently selected from alkyl, arylalkyl, cycloalkyl,
 alkenyl, cycloalkenyl, aryl, heteroaryl or
 cycloheteroalkyl;

R₃ is H or lower alkyl;

R₄ is H, halogen, CF₃, hydroxy, alkyl, alkoxy,
 20 alkanoylamino, aroylamino or cyano;

R₇ is H or lower alkyl;

and represents a single bond or a double bond
 (which may be cis or trans);

and pharmaceutically acceptable salts thereof (when
 25 R₃ is H), esters thereof, prodrug esters thereof, and all
 stereoisomers thereof.